Amendments to the Claims

Please cancel Claims 1 through 37 submitted in the previous Preliminary Amendment on November 30, 2004. Please amend the claims as follows:

1-37. Cancelled.

38. (New): A compound of Formula I

wherein:

A is $H-(Q)_{D}$ -;

Q is independently selected, each time taken, from the group amino acyl; p is an integer from 1 to 10;

X is O, S, SO, SO₂, or CR^3R^4 ;

 R^3 is fluoro, X'OR⁵, SO₃H, tetrazol-5-yl, CN, PO₃R⁶₂, hydroxy, NO₂, N₃, (CH₂)_mCOOR⁵a, (CH₂)_mPO₃R⁶a₂, NHCONHR⁵b, or NHSO₂R⁵c and R⁴ is hydrogen; or R³ and R⁴ each represent fluoro; or R³ and R⁴ together represent =O, =NOR⁷, =CR⁸R⁹, =CHCOOR⁵b, =CHPO₃R⁶a₂, or =CHCN; or one of R³ or R⁴ represents amino and the other represents carboxyl;

X' represents a bond, CH2, or CO;

m is an integer from 1 to 3;

R⁵, R^{5a}, R^{5b}, R^{5c}, R⁷, R⁸, and R⁹ are independently a hydrogen atom; an optionally substituted (1-6C) alkyl group; an optionally substituted (2-6C) alkynyl group; an optionally substituted aromatic group; an optionally substituted heteroaromatic group; a non-aromatic carbocyclic group; a non-aromatic heterocyclic group; a non-aromatic monocyclic carbocyclic group fused with one or two monocyclic aromatic

or heteroaromatic groups; or a non-aromatic monocyclic heterocyclic group fused with one or two monocyclic aromatic or heteroaromatic groups;

R6 and R6a independently represent hydrogen or a (1-6C)alkyl group;

R¹⁰ is hydrogen or fluoro; and

R¹¹ is hydrogen, fluoro, or hydroxy;

or a pharmaceutically acceptable salt thereof.

39. (New): A compound or salt according to Claim 38, provided that the compound or salt is not one in which X is CR^3R^4 wherein R^3 is fluoro and R^4 is hydrogen, p is 1, and Q is Lalanyl; or a pharmaceutically acceptable salt thereof.

40. (New): A compound or salt according to Claim 38 wherein

A is $H-(Q)_p$ -;

Q is independently selected, each time taken, from the group amino acyl;

p is an integer from 1 to 3;

 $X \text{ is } O, S, SO, SO_2, \text{ or } CR^3R^4;$

R³ is fluoro or hydroxy, and R⁴ is hydrogen; or R³ and R⁴ together represent =0;

R¹⁰ is hydrogen or fluoro; and

R¹¹ is hydrogen, fluoro, or hydroxy.

41. (New): A compound or salt according to Claim 39 wherein

A is $H-(Q)_{p}$ -;

Q is independently selected, each time taken, from the group amino acyl;

p is an integer from 1 to 3;

X is O, S, SO, SO₂, or CR^3R^4 ;

R³ is fluoro or hydroxy, and R⁴ is hydrogen; or R³ and R⁴ together represent =O;

R¹⁰ is hydrogen or fluoro; and

R¹¹ is hydrogen, fluoro, or hydroxy.

- 42. (New): A compound or salt according to Claim 38 wherein Q is an amino acyl derived from a natural amino acid.
- 43. (New): A compound or salt according to Claim 39 wherein Q is an amino acyl derived from a natural amino acid.
- 44. (New): A compound or salt according to Claim 40 wherein Q is an amino acyl derived from a natural amino acid.
- 45. (New): A compound or salt according to Claim 41 wherein Q is an amino acyl derived from a natural amino acid.
 - 46. (New): A compound or salt according to any one of Claims 38-45 wherein X is SO2.
- 47. (New): A compound or salt according to any one of Claims 38-45 wherein X is CR^3R^4 , R^3 is fluoro, and R^4 is hydrogen.
- 48. (New): A compound or salt according to any one of Claims 38-45 wherein X is CR^3R^4 , R^3 is hydroxy, and R^4 is hydrogen.
- 49. (New): A pharmaceutically acceptable salt according to Claim 38 that is an acid-addition salt made with an acid which provides a pharmaceutically acceptable anion; a base-addition salt made with a base which provides a pharmaceutically acceptable anion for a compound which contains an acidic moiety; or a zwitterionic compound which contains oppositely charged groups.
 - 50. (New): A compound according to Claim 38 wherein

A is $H-(Q)_p$ -;

Q is L-alanyl;

p is 1;

X is SO_2 or CR^3R^4 ;

R³ is fluoro and R⁴ is hydrogen;

R¹⁰ is hydrogen; and

R¹¹ is hydrogen;

or the hydrochloride salt, to sylate salt, mesylate salt, esylate salt, besylate salt, or monosodium salt thereof.

- 51. (New): The pharmaceutically acceptable salt according to Claim 50 which is $(1R,4S,5S,6S)-4-(2^{\circ}S-Aminopropionyl)$ amino]-2,2-dioxo-2 λ^6 -thia-bicyclo[3.1.0.]hexane-4,6-dicarboxylic acid hydrochloride or $(1R,4S,5S,6S)-4-(2^{\circ}S-2^{\circ}-Aminopropionyl)$ amino-2,2-dioxo- $2\lambda^6$ -thia-bicyclo[3.1.0.]hexane-4,6-dicarboxylic acid tosylate.
- 52. (New): The compound according to Claim 38 which is $(1R,4S,5S,6S)-4-(2^{\circ}S-4^{\circ}-methylthio-2^{\circ}-aminobutanonyl)$ amino-2,2-dioxo- $2\lambda^{6}$ -thia-bicyclo[3.1.0]hexane-4,6-dicarboxylic acid or a pharmaceutically acceptable salt thereof.
- 53. (New): The compound according to Claim 52 which is (1R,4S,5S,6S)-4- $(2'S-4'-methylthio-2'-aminobutanonyl)amino-2,2-dioxo-<math>2\lambda^6$ -thia-bicyclo[3.1.0]hexane-4,6-dicarboxylic acid monohydrate.
- 54. (New): The pharmaceutically acceptable salt according to Claim 38 that is 1S,2S,4S,5R,6R-2-(2'S-aminopropionyl)amino-4-hydroxy-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid hydrochloride.

55. (New): A compound according to Claim 38 wherein

A is $H-(Q)_{D}$ -;

Q is L-alanyl;

p is 1;

X is CR^3R^4 :

R³ is fluoro and R⁴ is hydrogen;

R¹⁰ is hydrogen; and

R¹¹ is hydrogen;

or a pharmaceutically acceptable salt thereof.

- 56. (New): The compound or salt according to Claim 55 which is selected from the group consisting of:
 - a) 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid hydrochloride;
 - b) 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate;
 - c) 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esylate;
 - d) 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid besylate;
 - e) 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2.6-dicarboxylic acid tosylate;
 - f) 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid; and
 - g) 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic monosodium salt.
- 57. (New): The pharmaceutically acceptable salt according to Claim 56 which is 1R,2S,4R,5R,6R-2-(2'S-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate.
- 58. (New): The pharmaceutically acceptable salt according to Claim 57 which is (1R,2S,4R,5R,6R)-2-(2'S-2'-aminopropionyl)amino-4-fluoro-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate monohydrate.
- 59. (New): A process for preparing a compound of Formula I, or a pharmaceutically acceptable salt thereof, as claimed in Claim 38 comprising acylating a compound of formula (ii)

with a corresponding amino acyl of Formula III

$$Pg^{N}-A$$
 (III)

wherein PgN is a nitrogen-protecting group;

whereafter, for any of the above procedures, when a functional group is protected using a protecting group, removing the protecting group;

whereafter, for any of the above procedures: when a pharmaceutically acceptable salt of a compound of Formula I is required, reacting the basic form of such a compound of Formula I with an acid affording a pharmaceutically acceptable counterion; or for a compound of Formula I which bears an acidic moiety, reacting the acidic form of such a compound of Formula I with a base which affords a pharmaceutically acceptable cation; or for a zwitterionic compound of Formula I, neutralizing the acid-addition salt form or base-addition salt form of such a compound of Formula I; or by any other conventional procedure.

- 60. (New): A method for affecting the cAMP-linked metabotropic glutamate receptors in a patient, which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 38.
- 61. (New): A method for affecting the cAMP-linked metabotropic glutamate receptors in a patient, which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 39.

62. (New): A method of administering an effective amount of a compound of Formula II,

wherein X and R¹⁰ are defined as in Claim 38,

which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 38.

63. (New): A method of administering an effective amount of a compound of Formula II,

wherein X and R¹⁰ are defined as in Claim 39,

which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 39.

- 64. (New): A method for treating a neurological disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 38.
- 65. (New): A method for treating a neurological disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 39.

- 66. (New): The method of Claim 64 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass and grafting; cerebral ischemia; spinal cord trauma; head trauma; Alzheimer's Disease; Huntington's Chorea; amyotrophic lateral sclerosis; AIDS-induced dementia; perinatal hypoxia; hypoglycemic neuronal damage; ocular damage and retinopathy; cognitive disorders; idiopathic and drug-induced Parkinson's Disease; muscular spasms; migraine headaches; urinary incontinence; drug tolerance, withdrawal, cessation, and craving; smoking cessation; emesis; brain edema; chronic pain; sleep disorders; convulsions; Tourette's syndrome; attention deficit disorder; and tardive dyskinesia.
- 67. (New): The method of Claim 65 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass and grafting; cerebral ischemia; spinal cord trauma; head trauma; Alzheimer's Disease; Huntington's Chorea; amyotrophic lateral sclerosis; AIDS-induced dementia; perinatal hypoxia; hypoglycemic neuronal damage; ocular damage and retinopathy; cognitive disorders; idiopathic and drug-induced Parkinson's Disease; muscular spasms; migraine headaches; urinary incontinence; drug tolerance, withdrawal, cessation, and craving; smoking cessation; emesis; brain edema; chronic pain; sleep disorders; convulsions; Tourette's syndrome; attention deficit disorder; and tardive dyskinesia.
- 68. (New): The method of Claim 66 or 67 wherein said neurological disorder is drug tolerance, withdrawal, cessation, and craving; or smoking cessation.
- 69. (New): A method for treating a psychiatric disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 38.
- 70. (New): A method for treating a psychiatric disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 39.

- 71. (New): The method of claim 69 wherein said psychiatric disorder is schizophrenia, anxiety and related disorders, depression, bipolar disorders, psychosis, and obsessive compulsive disorders.
- 72. (New): The method of claim 70 wherein said psychiatric disorder is schizophrenia, anxiety and related disorders, depression, bipolar disorders, psychosis, and obsessive compulsive disorders.
- 73. (New): The method according to any one of Claims 71 or 72 wherein said psychiatric disorder is anxiety and related disorders.
- 74. (New): A pharmaceutical formulation comprising in association with a pharmaceutically acceptable carrier, dilutent or excipient, a compound of Formula I, or a pharmaceutically acceptable salt thereof.